

HORST LINDHOFER et al.

PATENT

Application No.: 09/094,921, Group Art Unit: 1642, Examiner: Holleran, A.

Amendment No. 3 -- Page 5

72 human-IgG1/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG4-  
73 [CH2]-human-IgG3\*-[CH3]  
74 human-IgG4/human-[VH-CH1,VL-CL]-human-IgG4-[hinge]-human-IgG4-  
75 [CH2]-human-IgG3\*-[CH3]  
76 rat/mouse.

C2 1 20. (twice amended) Method according to claim 1, in which said bispecific antibodies are  
2 added in an amount of 2 to 100 µg.

#### REMARKS

The recitations added to claim 1 are taken from claim 22, now deleted. No new matter is presented. Entry of this amendment and reconsideration of the application are respectfully requested.

Respectfully submitted,



M. Henry Heines  
Reg. No. 28,219

TOWNSEND and TOWNSEND and CREW LLP  
Two Embarcadero Center, 8<sup>th</sup> Floor  
San Francisco, California 94111-3834  
Tel: (415) 576-0200  
Fax: (415) 576-0300  
MHH  
SF 1262071 v1

**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

1. (twice amended) Method for the preparation of a vaccine for immunization of humans and animals against tumor cells comprising the steps of:

- a) isolating autologous tumor cells;
- b) treating the tumor cells to prevent the survival thereof following reinfusion;
- c) incubating the thus treated tumor cells with intact heterologous bispecific [~~and/or~~  
~~trisp~~pecific] antibodies showing the following properties:

$\alpha$  - binding to a T cell;

$\beta$  - binding to at least one antigen on a tumor cell;

$\gamma$  - binding, by their Fc portion [~~(in the case of bispecific antibodies), or by a third~~  
~~specificity (in the case of trisp~~pecific antibodies)] to Fc receptor-positive cells

**capable of activating the Fc receptor-positive cell whereby the expression of  
cytokines, co-stimulatory antigens or both is induced or increased,** wherein

the bispecific antibodies are members selected from the group consisting of the following isotype combinations:

rat-IgG2b/human-IgG1,

rat-IgG2b/human-IgG2,

rat-IgG2b/human-IgG3[oriental allotype G3m(st) = binding to protein A],

rat-IgG2b/human-IgG4;

rat-IgG2b/rat-IgG2c;

mouse-IgG2a/human-IgG3[caucasian allotypes G3m(b+g) = no binding to protein A, in the following indicated as \*]

mouse-IgG2a/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-  
human-IgG3\*-[CH2-CH3]

mouse-IgG2a/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3\*-[CH2-CH3]

mouse-IgG2a/human-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3\*-[CH2-CH3]

mouse-[VH-CH1,VL-CL]-human-IgG1/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3\*-[CH2-CH3]

mouse-[VH-CH1,VL-CL]-human-IgG4/rat-[VH-CH1,VL-CL]-human-IgG4-[hinge]-human-IgG4[N-terminal region of CH2]-human-IgG3\*[C-terminal region of CH2: > aa position 251]-human-IgG3\*[CH3]

rat-IgG2b/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge-CH2-CH3]

rat-IgG2b/mouse-[VH-CH1,VL-CL]-human-IgG2-[hinge-CH2-CH3]

rat-IgG2b/mouse-[VH-CH1,VL-CL]-human-IgG3-[hinge-CH2-CH3, oriental allotype]

rat-IgG2b/mouse-[VH-CH1,VL-CL]-human-IgG4-[hinge-CH2-CH3]

human-IgG1/human-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3\*-[CH2-CH3]

human-IgG1/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG4[N-terminal region of CH2]-human-IgG3\*[C-terminal region of CH2 : > aa position 251]-human-IgG3\*[CH3]

human-IgG1/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG4[N-terminal region of CH2]-human-IgG3\*[C-terminal region of CH2 : > aa position 251]-human-IgG3\*[CH3]

human-IgG1/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG2[N-terminal region of CH2]-human-IgG3\*[C-terminal region of CH2 : > aa position 251]-human-IgG3\*[CH3]

human-IgG1/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG2[N-terminal region of CH2]-human-IgG3\*[C-terminal region of CH2 : > aa position 251]-human-IgG3\*[CH3]

human-IgG1/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3\*-[CH2-CH3]

human-IgG1/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3\*-[CH2-CH3]

human-IgG2/human-[VH-CH1,VL-CL]-human-IgG2-[hinge]-human-IgG3\*-[CH2-CH3]

human-IgG4/human-[VH-CH1,VL-CL]-human-IgG4-[hinge]-human-IgG3\*-[CH2-CH3]

human-IgG4/human-[VH-CH1,VL-CL]-human-IgG4-[hinge]-human-IgG4[N-terminal region of CH2]-human-IgG3\*[C-terminal region of CH2 : > aa position 251]-human-IgG3\*[CH3]

mouse-IgG2b/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3\*-[CH2-CH3]

mouse-IgG2b/human-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3\*-[CH2-CH3]

mouse-IgG2b/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3\*-[CH2-CH3]

mouse-[VH-CH1,VL-CL]-human-IgG4/rat-[VH-CH1,VL-CL]-human-IgG4-  
[hinge]-human-IgG4-[CH2]-human-IgG3\*-[CH3]

human-IgG1/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG4-[CH2]-  
human-IgG3\*-[CH3]

human-IgG1/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG4-  
[CH2]-human-IgG3\*-[CH3]

human-IgG4/human-[VH-CH1,VL-CL]-human-IgG4-[hinge]-human-IgG4-  
[CH2]-human-IgG3\*-[CH3]

rat/mouse.

20. (twice amended) Method according to claim 1, in which said bispecific [or trispecific] antibodies are added in an amount of 2 to 100  $\mu$ g.